REMARKS

The Examiner is thanked for entry of the April 11, 2009 amendment and the prompt advisory action. Claims 1-2 and 7-12 are pending in the application.

The Examiner is further thanked for the indication that claim 9 would be allowable if rewritten in independent form. Accordingly, claims 7-9 has been canceled and their limitations incorporated into claim 1. Claims 11 and 12 have also been amended and new claims 20-28 are presented. No new matter has been added.

In light of the claim amendments and the following remarks, Applicant respectfully requests that the Examiner withdraw the rejections and pass this case to issuance.

Priority

The Office Action states that application serial nos. 60/116,748, 60/127,142 and parent application no. 09/491,896 fail to provide an enabling disclosure for the invention claimed in claims 1, 2, 4-12 and 14. Applicant disagrees with this assessment, and submits that the priority documents do provide adequate support for the claims under 35 U.S.C. § 119(e) and 120. The Examiner is thanked for the acknowledgement on page 3 of the June 11, 2009 Office Action that "the priority issue stands or falls with the enablement rejection." Since *composition* claims 1-2 and 10 are now in condition for allowance, enablement is discussed below with regard to *method* claims 11-12 and 20-28.

Amendments to the Claims

As noted above, composition claim 1 has been amended to incorporate the limitations of claim 9 and intervening claims 7-8. Accordingly, claims 7-9 are canceled.

Method claim 11 has likewise been amended to incorporate the substantive features of claim 9 (i.e., the use of an adeno-associated vector) and is also believed to be in condition for allowance for the same reason as amended claim 1.

Method claim 12 have been amended to replace the word "vector" with "composition." New claims 20-28 are presented to claim various delivery systems for the genetic vaccines

disclosed by the Applicant. Support for the amendment to claim 12 and new claims 20-28 can be found throughout the specification and in, for example, in section I ("Genetic Vaccines") on pages 15-22 and Section IV ("Delivery Systems") – paragraphs [0083-0110] and [0134-0148] of the published application.

Rejection Under 35 U.S.C. §103(a)

Claims 1-2, 7-8 and 10 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lissin *et al.* (PNAS 95: 7097-7102 (1998)) in view of Kammescheidt et al. (1996). The amendments to claim 1 to incorporate allowable subject matter of claim 9 render the obviousness grounds for rejection moot.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1, 2 and 7-12 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification "does not reasonably provide enablement for a composition comprising any vector encoding any NMDA receptor antigen, nor for a method of modulating or delaying onset of epilepsy, stroke, or decreased cognition in any subject, by administration of any vector encoding any NMDA receptor antigen." Each of these issues is discussed below.

"Any NMDA receptor antigen"

The August 11, 2009 amendments addressed this issue by amending each of the independent claims to specify *an NMDA receptor-1 antigen*. Since the Examiner has already acknowledged (on page 3 of the June 11, 2009 Office Action) that the claims are enabled for the NMDAR-1 antigen, this ground for rejection is now moot.

"Any subject"

Since the composition claims 1-2 and 10 currently stand allowable, the scope of enablement is only pertinent to the pending methods claims and Applicant again assert that specification while only presenting experimental results in rats is enabling for the broader scope of subjects as defined in the specification, including humans. The Examiner is reminded of the standard stated in the MPEP 2164.02, "[a]n *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a

disclosed or claimed method invention." Thus, an animal model is acceptable where it is recognized in the art that this model correlates to a specific condition.

The Applicant has demonstrated the claimed invention in animal models accepted by those in the skilled in the art. In fact, following the filing of this application, Applicant's work was published in the peer-reviewed journal, *Science*, further demonstrating the animal models presented in the application were indeed accepted by those skilled in the art. See. During et al. "*An Oral Vaccine Against NMDAR1 with Efficacy in Experimental Stroke and Epilepsy*," Science Vol. 287 1453-1460 (February 25, 2000), attached hereto as an appendix.)

Mode of administration

Since the composition claims 1-2 and 10 currently stand allowable, the scope of enablement is again only pertinent to the pending methods claims. While only presenting experimental results with an *oral composition*, the specification fully enables other modes of administration as well. See, for example, Section III ("Pharmaceutical Compositions and Pharmaceutical administration") – paragraphs [0120-0133] of the published application and Section IV ("Delivery Systems") – paragraphs [0134-0148] of the published application, in which alternative delivery mechanisms such as intravenous and intramuscular injection are taught in detail.

The Examiner has cited the McCluskie article (McCluskie et al. (1999) Mol. Med. 5:287-300) as the principal basis for her enablement rejection, noting that:

> ...McCluskie et al. only observed antibody responses to injected routes of administration of DNA vaccines and not to non-injected routes of administration of DNA vaccines, such as oral routes, sublingual, inhalation and vaginal wall because of variation in transfection efficiency (Abstract).[1]

In response Applicant notes that the full McCluskie article (as opposed to the sentence taken out of context from the Abstract) supports the enablement of Applicant's claims. The McCluskie article demonstrates that at the time of invention (1999) various modes of genetic

[1] See page 10 of the November 21, 2005 Office Action.

vaccine administration such as intravenous injection, intramuscular, gene-gun and non-injected administration were well known to one skilled in the art.

The suggestion that McCluskie's article makes the results "unpredictable" is not supported by the article. McCluskie demonstrated humoral responses to genetic vaccines in four different *injectable* modes of genetic vaccine administration (intravenous, intramuscular, sublingual and intradermal) while not observing a response to oral administration. McCluskie's experiments were designed such that the same dose was administered regardless of mode of administration so it should not be at all surprising that at the chosen dose injectable modes induced antibody formation while non-injected modes did not. Selecting an optimal dose is well within the capabilities of one skilled in the art.

Moreover, unlike McCluskie, Applicant has demonstrated a humoral response *via oral administration* so there is no reason to suspect that *injectable modes* of administration would be *less* effective.

Any vector

The Examiner again asserts that the invention is only enabled for use with an adeno-associated virus vector. Applicant disagrees that the claims are not enabled for different vectors.

One skilled in the art would be familiar with the ability to make and use the composition of claim 1 with any vector recited in section IV "Delivery Systems" of the specification, paragraphs [0135]-[0148]. In fact, the Examiner even states in the Advisory Action on page 4 that "it is unclear why the *adenovirus* vector of Lissen would not be suitable for eliciting production of NMDA receptor-1 antibodies."

In fact, as Applicant has stated previously, one of ordinary skill in the art having familiarity with AAV vectors would have knowledge to make and use other vectors or delivery compositions, in general. The general knowledge is complemented by Section IV of the Application.

In summary, the Examiner bears the burden of establishing a basis for questioning enablement. See MPEP 2164.04. Despite numerous office actions, a reasonable basis for rejecting the scope of Applicant's method claims, especially claim 12, has not been presented.

CONCLUSION

In view of the above remarks, Applicant' respectfully requests reconsideration and allowance of the application. The Examiner is invited to call the undersigned at (617) 439-2948 if there are any questions. In the event that the amendments do not place this case in condition for allowance, entry of the amendments and a further advisory action are requested to facilitate appeal.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 141449, under Order No. 106604-7.

Dated: November 12, 2009

Respectfully submitted,

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